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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/814,604	03/22/2001	Elliott S. Klein	P-AR 4528	4120

23601 7590 11/24/2004

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/814,604	KLEIN ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/25/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-26 are pending and under consideration.

Response to Amendment

The objection to the Specification has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 1-3, 6-8, 11-13, 16, 19 under 35 U.S.C. 102(b) as being anticipated by Chen et al. (1995) has been withdrawn.

The rejection of claims 1-3, 6-8, 11-16, 18-19 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (1995) in view of Chen et al. (1996) has been withdrawn.

New and remaining issues are set forth below.

Specification

According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. A sequences appears on page 19, line 25, of the specification but are not identified by SEQ ID NO as required.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying agents which dissociate a nuclear hormone test complex comprising a nuclear hormone receptor dimer, a coactivator and a corepressor in vitro, does not reasonably provide enablement for methods of identifying agents which dissociate a nuclear hormone test complex comprising a nuclear hormone receptor dimer, a coactivator and a corepressor in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to methods of identifying agents that dissociate a nuclear hormone test complex comprising a nuclear hormone receptor dimer, a coactivator and a corepressor. The claims are not limited to in vitro use, and thus the claims as written encompass in vivo methods. However, the specification does not adequately teach how to effectively practice the method in vivo. While the Specification asserts that expression of a nucleic acid molecule encoding a nuclear hormone receptor is well known in the art, the art teaches that numerous factors complicate *in vivo* gene expression with respect to predictably achieving levels and duration of gene expression which have not been shown to be overcome by routine experimentation, see Eck & Wilson. This reference teaches that complicating factors include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of

altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. Eck and Wilson, page 82, column 1, first paragraph. These factors differ dramatically based on the protein being produced. As such, in light of the state of the art for in vivo gene expression, the specification fail to provide guidance for any of the above parameters for *in vivo* gene expression.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record set forth in the Office Action of 3/8/2004.

Claims 1, 2, 11 and 18 are vague and indefinite in the recitation of the term "activities". This term is not clearly defined in the claims. The specification also does not clearly define the term, but it seems to include, *inter alia*, an indirect signaling pathway activated by the nuclear hormone receptor, and on other nuclear hormone receptor mediated pathways (page 9, lines 5-20), and also a decrease in interaction with corepressors and an increase in interaction with coactivators (page 14, lines 10-20). Thus, since the term "activities" includes effects on indirect pathways not directly associated with nuclear hormone receptor function, the skilled artisan would not be apprised of the metes and bounds of the functional limitation with regard to the

activities which are dissociated. Claims 3-10, 12-17, 19-26 are rejected insofar as they depend on the recitation of the term "activities" in claims 1, 2, 11, 18

Applicant argues that the meaning of the term "nuclear hormone receptor activities" is clear to the skilled person in view of the specification, and that nuclear hormone receptor activities are those activities resulting from activation of a pathway by a nuclear hormone receptor, and that therefore, in contrast to the assertion in the Office Action, these activities are all associated with nuclear hormone receptor function. Applicant points to the specification at page13, lines 24-31, which discloses an indirect signaling pathway activated by the nuclear hormone receptor. However, The specification teaches, for example, that ligands that dissociate nuclear hormone receptor activities have selective indirect effects through nuclear hormone receptor-mediated pathways while failing to directly activate transcription through cognate response element (page 9, lines 2-13). The metes and bounds of this term cannot be determined based upon the definition provided in the Specification because the activities ascribed to the nuclear hormone receptor are exemplary, and further there is no indication what the indirect effects would be.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The

examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 16, 2004

JOSEPH MURPHY
PATENT EXAMINER